

IN THE CLAIMS

1. (Previously Presented) An aspartic enzyme that produces plasma protein fragments having an inhibitory activity to metastasis and growth of cancer.

2. (Currently Amended) The enzyme that produces plasma protein fragments of claim 1, which has the following properties:

- (a) it has a molecular weight of about 45 kDa as measured by SDS electrophoresis under non-reduced condition;
- (b) it has the N-terminal amino acid sequence LVR IPLHKFT (SEQ ID NO:1);
- (c) it degrades plasma proteins at an acidic pH range of not more than pH 5.0 to produce plasma protein fragments having an inhibitory activity to metastasis and growth of cancer; and
- (d) it is an aspartic enzyme having N-terminal amino acid sequence homology to a cathepsin D precursor.

3. (Original) The enzyme that produces plasma protein fragments of claim 1 or 2 wherein said plasma proteins to be fragmented are selected from the group consisting of plasminogen, fibronectin, vitronectin and human hepatocyte growth factor (HGF).

4. (Previously Presented) The enzyme that produces plasma protein fragments of claim 1 wherein said enzyme cleaves plasminogen at 73L-74F and/or 451L-452P to produce fragments comprising Kringles 1 to 4 of plasminogen.

5. (Withdrawn - Previously Presented) Plasma protein fragments that are produced from degradation by the action of the enzyme that produces plasma protein fragments as set forth in claim 1 and have an inhibitory activity to metastasis and growth of cancer.

6. (Withdrawn) The plasma protein fragments of claim 5 that are derived from plasma proteins selected from the group consisting of plasminogen, fibronectin, vitronectin and human hepatocyte growth factor (HGF).

7. (Withdrawn) The plasma protein fragments of claim 5 or 6 comprising Kringles 1 to 4 plasminogen.

8. (Withdrawn) The plasma protein fragments of claim 5 or 6 comprising heparin-binding domain of fibronectin.

9. (Withdrawn-Previously Presented) A process for preparing plasma protein fragments having an inhibitory activity to metastasis and growth of cancer, which comprises reacting plasma protein fragments as set forth in claim 1.

10. (Withdrawn) The process of claim 9 wherein said process further comprises specifically isolating the plasma protein fragments having an inhibitory activity to metastasis and growth of cancer with a resin having a heparin carrier.

11. (Previously Presented) A medicament for treating solid cancer comprising as a major ingredient the enzyme that produces plasma protein fragments as set forth in claim 1.

12. (Cancelled)

13. (Withdrawn-Previously Presented) A medicament for treating and preventing disease conditions associated with vascularization such as cancer (solid cancer), diabetic retinosis and rheumatism comprising as a major ingredient the plasma protein fragments as set forth in claim 5.

14. (Withdrawn-Previously Presented) A medicament for treating and preventing cancer comprising as a major ingredient the plasma protein fragments as set forth in claim 5.

15. (Previously Presented) The enzyme of claim 2, wherein the plasma protein fragments have a molecular weight of 40 or 43 kDa comprising Kringle 1 to Kringle 4.

16. (Previously Presented) The enzyme of claim 1, wherein said enzyme is active at a pH of not more than 5.0.

17. (Previously Presented) An aspartic enzyme that produces plasma protein fragments having an inhibitory activity to metastasis and growth of cancer wherein said enzyme is active in an acidic pH range and which is inhibited by an aspartic protease inhibitor.